2002/2003 MSPPSA SERIES

DNA AMPLIFICATION INSTRUMENTATION

AN ANALYSIS OF MARKET SIZE & GROWTH MARKET SHARE PURCHASE PLANS & SUPPLIER ASSESSMENT FOR THE U.S. LIFE SCIENCE RESEARCH MARKET

A Multi-Client Report

by
PhorTech International
San Carlos, California

May 8, 2002

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I. Background

A. SURVEY OBJECTIVES

The purpose of this survey was to provide the management of our client companies with an analysis of the current market for DNA amplification instrumentation (including the installed base of platforms for real-time quantitative PCR and thermal cyclers) in the U.S. and of the attitudes and expectations of a cross-section of researchers who utilize DNA amplification in their work. Due to the size of the survey, expanded this year to include a dedicated section on real-time quantitative PCR and a more detailed examination of thermostable enzyme usage, thermostable enzyme usage will be examined in a companion report entitled DNA Amplification Reagents & Methodology.

The surveying was blind, with no reference made to any clients for the survey. To encourage respondents to express themselves freely, the survey was anonymous, and made frequent use of open-ended questions.

Several demographic screens were used to characterize respondents, including scientific discipline, type of organization and length of experience with DNA amplification. Each respondent was characterized also by the applications for which he employs DNA amplification.

Early on in the survey, respondents were asked whether or not they currently use PCR, cycle sequencing, real-time PCR or other DNA amplification techniques in their work. Those respondents who answered positively were asked to provide the number of people in their group. These were then directed to the section regarding current usage of real-time quantitative PCR, a new addition for this year.

First, respondents were asked to indicate which of four choices (confirmation of screening data, gene expression, quantitation of cells or viruses, SNP genotyping) or a fifth optional 'other' category best represents the applications using this type of instrumentation. Respondents were then directed to a detailed audit question. Specifically, researchers were asked to itemize the brand and model, along with the sample capacity, quantity owned, year acquired and approximate cost for each real-time quantitative PCR platform to which they have access. Respondents were also asked to provide their throughput in runs per month and the number of reactions per run. Next, given six choices of methods for monitoring assays plus a seventh write-in option, respondents were asked to indicate the percentage of reactions for which they utilize each method. Queries regarding the proportion of reactions which are multiplexed and the fluorophores used with these assays complete this section.

Users were next asked a comparable series of questions regarding their usage of thermal cyclers for techniques other than real-time quantitative PCR. In particular, respondents were asked to indicate both the throughput of PCR runs per month and the number of reactions per run. They were then directed to a detailed audit of these thermal cyclers. Similar to that for real-time quantitative PCR platforms, here respondents were asked to itemize all thermal cyclers used for all other techniques which they owned or operated, providing the brand, model, sample capacity, date acquired, and cost for each unit.

Respondents were questioned regarding their reasoning behind choosing their last thermal cycler, whether they would choose this unit again and were asked to explain their reasons. For those who indicated that they would not make the same decision again, we requested more specific additional information regarding the brand, model and sample capacity of the thermal cycler which would be purchased instead. Respondents were also queried as to their current purchasing plans and asked to provide the brands and models of thermal cyclers under consideration.

Users were next asked to select the highest-rated manufacturer in six key areas. In particular, respondents were asked to choose the top-ranked supplier among seven leading thermal cycler manufacturers (or an eighth choice indicating an 'other' brand) in the following areas: ease of use, most reliable quality, level of tech/application support, innovation, value for money, and commitment to the field. They were then asked to detail desired improvements or added features they would like to see in thermal cyclers.

The second section of the survey largely consists of questions regarding the usage of thermostable enzymes which will be presented in the upcoming report, DNA Amplification Reagents & Methodology. This will include respondents' consumption of thermostable enzyme kits and separate enzymes for eight different procedures. Preferred nucleotide suppliers, preferences for reagents, kits and master mixes will be examined, as will their level of satisfaction with enzyme suppliers.

However, two questions from this second section will be included here. The first identifies the type of PCR reaction container used most often from a list of eight options. These are 0.5 ml thin walled, 0.5 ml standard, 0.2 ml thin walled, 0.2 ml standard, a slide, 96 well plate, a 384 well plate or 'other' type. Finally, in the last question on the survey, respondents indicate which of eleven improvements would be most important to their work. Choices here include higher fidelity, higher yield, less cycling time, longer amplicons, better sensitivity, higher specificity, less set-up time, the capability to perform real-time analysis, less reagent consumption, room temperature assembly, or

minimal optimization. Alternatively, researchers could write-in an unlisted improvement.

Major objectives of the survey were to estimate the present size of the markets for real-time quantitative PCR platforms and for thermal cyclers used for all other techniques. For each category of instrumentation, we will also determine the present market share for leading companies in the U.S. based upon the installed base of units, to measure the market's historic growth rate, based upon the identified installed base, to identify the leading suppliers in terms of units placed and estimated dollar sales volume, and to segment DNA amplification users by application category. Finally, profiles of respondents most likely to purchase new instrumentation in the near term would be carefully examined.

In addition, respondents' satisfaction with instrumentation will be presented along with characteristics of work in the relatively new field of real-time quantitative PCR.

The audits should permit the evaluation of our clients' present market positions, identify marketing strengths and weaknesses, and suggest strategies to develop or improve sustainable competitive advantage.

This report is the first 2002/2003 study in a growing series of market research analyses that began in 1993. We plan to continue the series, adding titles and alternating between U.S. and international markets, depending upon our clients' suggestions and support.

Reports planned to be released in the 2002/2003 series include the following U.S. topics:

DNA Amplification Instrumentation
DNA Amplification Reagents & Methodology
Microplate Reader & Equipment Market

Topics in the U.S. series published in 2001/2002 include:

Electrophoretic Instrumentation & Reagents
Molecular Biology Reagent Systems, Vol. 2

This series also includes the following reports covering international markets:

Densitometers & Image Analysis in Europe
DNA Sequencing in the Far East.

The 2000/2001 series covered the following three reports:

U.S. DNA Amplification
U.S. Molecular Biology Reagent Systems, Vol. 1
Molecular Biology Reagent Systems, Vol. 1 in the Far East.

In the 1999/2000 series, we have released three reports examining the following markets. These are:

Microplate Equipment in Europe
DNA Sequencing in the U.S.
Monoclonal Antibodies in the U.S.

The following nine titles have been released in the series for 1998/1999:

Cell & Tissue Culture in the U.S.
Cytokines & Growth Factors in the U.S.
DNA Amplification in the Far East
DNA Sequencing in Europe
Electrophoretic Gel Media in Europe
HPLC in the Life Sciences in the U.S.
Molecular Biology Reagent Systems, Vol. 1
Molecular Biology Reagent Systems, Vol. 2 in the Far East
Protein Expression Systems in the U.S.

The following titles have been released in the U.S. series for 1997/8:

DNA Sequencing
Molecular Biology Reagent Systems, Vol. 1
Molecular Biology Reagent Systems, Vol. 2
Molecular Diagnostics.

Clients are reminded that additional copies of any of these reports that have been purchased in the past are available at a modest cost. Please contact us for further details. Those wishing to know publication dates for any of these reports, or wanting to read summaries of the 72+ reports in this series are invited to visit our Web site at: www.phortech.com.

B. SURVEY METHODOLOGY

E-mail invitations to take part in the survey were sent to a selected cross-section of life science researchers from our panel of over 5,000 U.S. life science researchers. After selection for appropriate areas of interest, invitations were sent to a random selection of 1,542 U.S. members of the panel who have been in contact with us in the last year. Customized e-mail invitations to the web site survey were sent to the selected individuals on February 26th, 2002.

Each participant received an e-mail invitation including the web address of the survey and a unique validation code.

To improve response rates, respondents were able to select from a choice of five prizes for completing the survey. These were a custom designed tee shirt, a chest of Ferrero Rocher chocolates, a laser pointer, a 120 minute MCI phonecard, an electronic stopwatch, a stainless steel folding knife, or a $5 gift card good towards any purchase at Barnes & Noble.

The questionnaires were anonymous, using a combination of tabular entry, check-offs, and open-ended probes. However, the majority of respondents did identify themselves by filling in the prize form. This made it possible for us to double-check the responses to some questions by telephoning respondents, improving the overall confidence in the data.

Undeliverables to the PhorTech database mailing were measured at 89 or 5.8% By the close of the survey on March 4th, 2002, we had received 438 responses to the first half of the survey on instrumentation and 386 responses to the reagent section. After removing duplicate responses and non-users, the final dataset contains a total of 412 valid responses regarding amplification instrumentation and 378 reporting thermostable enzyme data. This translates to an 30.1% response rate for the instrumentation section, and 26.6% for the reagent section. This exceeded our expectations.

We did not observe any survey fatigue in this questionnaire, and felt that respondents spent considerable time explaining their positions on the open-ended questions. We have no reason not to believe that the survey is representative of the entire U.S. population of DNA amplification users.

Based upon 412 responses describing DNA amplification instrumentation, the overall statistical results presented in this report are accurate to within ± 4.8 percentage points at the 95% confidence level. In cases where we only calculate the percentage of the 124 respondents currently using real-time quantitative PCR, the statistical results are accurate to within ± 8.8%.

In our experience, 95% confidence levels are appropriate primarily for scientific experiments. Most business people making decisions are content to be right more often than they are wrong. In this case, a 65% confidence level, (in which you would be right twice as often as you would be wrong) is appropriate. Conveniently, 65% confidence levels are nearly exactly one half the size of the 95% level, thus our 65% levels would be ± 2.4% for all respondents and ± 4.4% for all real-time quantitative PCR users.

According to the binomial distribution theory, these values are valid when the measured event has about a 50% probability. When the measured event is considerably more rare than this, the corresponding confidence intervals get smaller. On the other hand, these confidence intervals are valid for answers based upon the complete pool of respondents. When analyzing data for a group that includes only a small segment of respondents, the answers are less certain and confidence intervals are correspondingly larger.

In the report, we will calculate more exact individual confidence intervals when appropriate. In our comments, we will note whether given differences are significant at either the 65% or 95% level. To aid our clients in determining the appropriate confidence interval for various combinations of sample size and measurements, we have created the following table. Just read the closest percentage on the left and find the closest sample size column. The intersection will show the confidence interval for that combination. For example, a measured 35% value with a sample size of 200 has a 95% confidence interval of ± 6.6%.

95% Confidence Intervals for Various Percentages & Sample Sizes

Percent	n=10	n=20	n=50	n=100	n=200	n=500	n=1000
5%	±13.5%	±9.6%	±6.0%	±4.3%	±3.0%	±1.9%	±1.4%
10%	±18.6%	±13.1%	±8.3%	±5.9%	±4.2%	±2.6%	±1.9%
20%	±24.8%	±17.5%	±11.1%	±7.8%	±5.5%	±3.5%	±2.5%
35%	±29.6%	±20.9%	±13.2%	±9.3%	±6.6%	±4.2%	±3.0%
50%	±31.0%	±21.9%	±13.9%	±9.8%	±6.9%	±4.4%	±3.1%
65%	±29.6%	±20.9%	±13.2%	±9.3%	±6.6%	±4.2%	±3.0%
80%	±24.8%	±17.5%	±11.1%	±7.8%	±5.5%	±3.5%	±2.5%
90%	±18.6%	±13.1%	±8.3%	±5.9%	±4.2%	±2.6%	±1.9%
95%	±13.5%	±9.6%	±6.0%	±4.3%	±3.0%	±1.9%	±1.4%

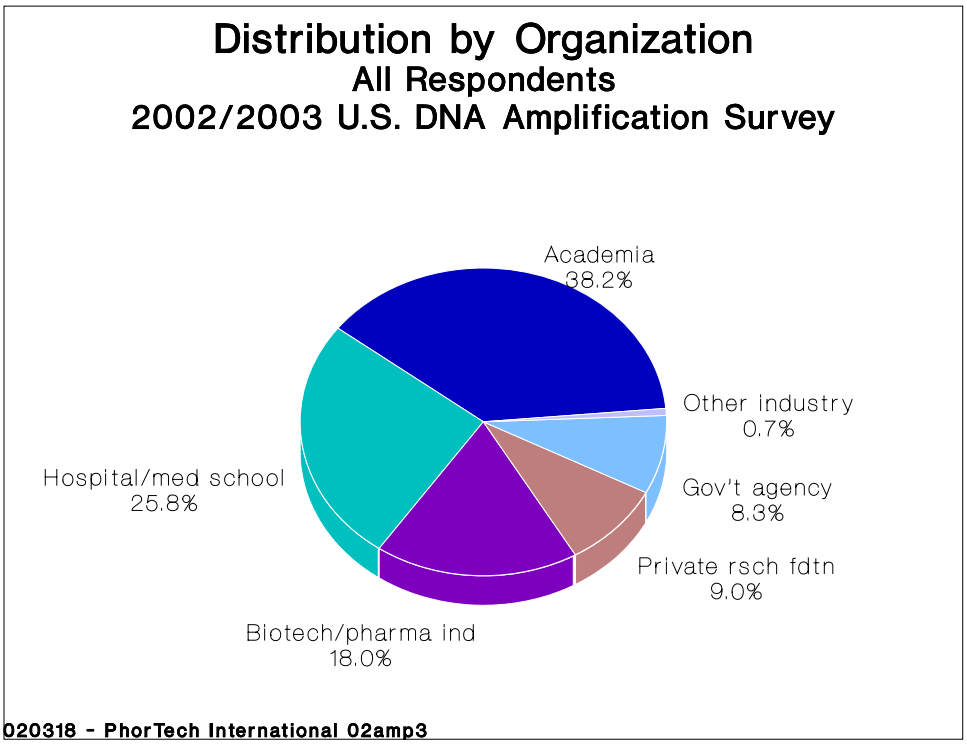
II. Demographic Segmentation

QUESTION 3.

Question:
How would you best describe your organization *(Best single answer):* Academia, Hospital/med school, Biotech/pharma industry, Other industry, Government agency, or Private research foundation?

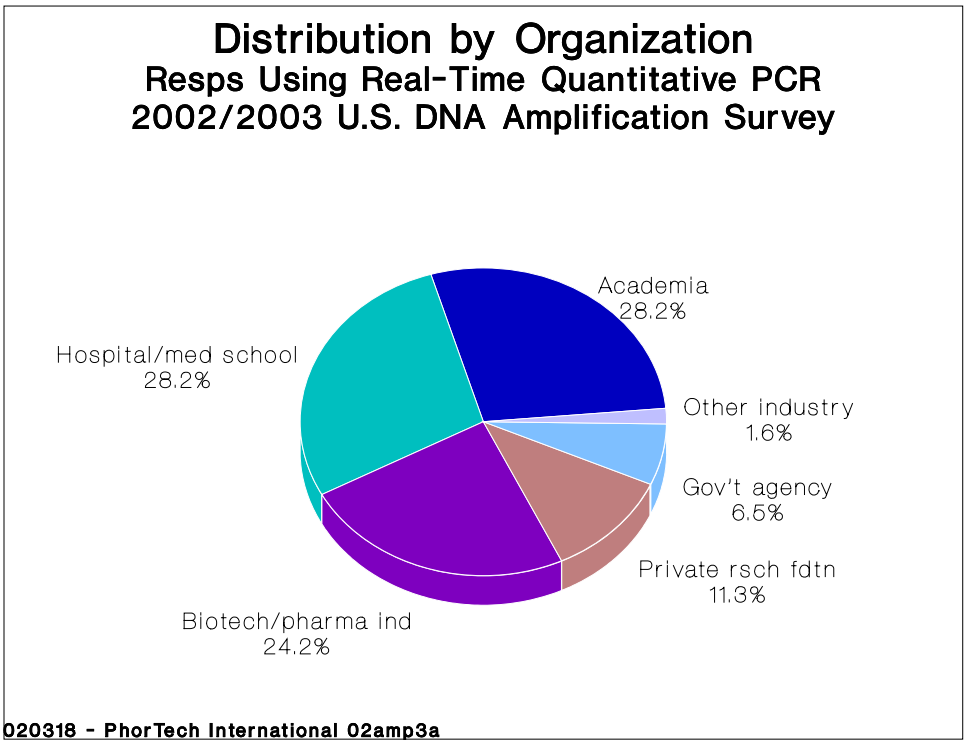
Rationale:
This question allows us to examine the distribution of respondents over the six types of organizations listed. This will identify where our respondents are located, and the primary sources of funding for current DNA amplification.

Results:
Before analyzing, the data required some editing in order for responses to be consistent. In order to reflect the source of funding, those working in a hospital, medical school or health science center have all been categorized as a hospital or medical school. Researchers working in private research foundations, many of which have an email ending in .org, and those receiving private funding from organizations such as HHMI, have been classified as private research foundations. VA Medical Centers and military organizations are considered to be government agencies. The distribution of responses from 411 of the 412 respondents to this survey are shown in the following pie chart.



Respondents located in academia represent nearly 40% of the DNA amplification users who responded to this survey with an additional 25% working in hospitals or medical schools. Researchers from the biotechnology or pharmaceutical industry sector account for nearly 20% while the remaining are split fairly equally between private research foundations and government agencies. Consistent with previous surveys covering this and various other areas of life science research, the representation by industries outside the biotechnology or pharmaceutical field is very small. Overall, this distribution is remarkably similar to those from our previous surveys of respondents using this technique.

In the following pie chart, we present the comparable distribution for the 124 researchers reporting owning or operating a real time quantitative PCR platform.



Compared to all respondents, it is perhaps not surprising to see that a larger proportion of organizations owning the very expensive real-time PCR platforms are located in the biotechnology or pharmaceutical industrial sector. This is accompanied by a drop in the share for academia resulting in 80% of these researchers split relatively evenly between academia, hospitals or medical schools and biotechnology or pharmaceutical industries.

Analysis:

Finally, for completeness, we present a list of the organizations represented by the respondents to this survey. These are first sorted according to the type of organization, with the largest sector, academia, listed first, and then presented in alphabetical order.

Organizations Represented by Respondents to this Survey

Academia
Ashland University
Auburn University
Boston University
Brandeis University
Bucks County Community College
California State University, Long Beach
Cancer Research Center of Hawaii
Columbia University
Cornell University
Creighton University
East Carolina University
Emory University
Harvard Dental School
Harvard University
Iowa State University
Johns Hopkins University
Louisiana State University
Marshall University
Massachusetts Institute of Technology
Miami University
Michigan Tech University
Montana State University
Moss Landing Marine Laboratories
North Carolina State University
Northwestern University
Ohio State University, Columbus
Ohio University
Oklahoma Animal Disease Diagnostic Laboratory
Oregon State University
Penn State University
Purdue University
Rockefeller University
Saint Louis University
San Diego State University
Southern Illinois University
Stanford University
State University of New York, Buffalo
SUNY at Buffalo
Tufts University
University of Alabama, Birmingham

University of Alberta
University of Arizona
University of Arkansas, Monticello
University of California, Davis
University of California, Los Angeles
University of California, Los Angeles/VAGLAHS
University of California, San Diego
University of California, San Francisco
University of Chicago
University of Cincinnati
University of Connecticut
University of Delaware
University of Denver
University of Florida
University of Florida, McKnight Brain Institute
University of Georgia
University of Illinois, Chicago
University of Illinois, Urbana
University of Illinois, Urbana-Champaign
University of Iowa
University of Kentucky
University of Louisiana, Monroe
University of Maryland Biotechnology Institute
University of Miami, Biochem
University of Michigan
University of Minnesota
University of Missouri
University of Montreal
University of Nebraska, Lincoln
University of New Mexico
University of North Carolina, Chapel Hill
University of Pennsylvania
University of Pittsburgh
University of Puerto Rico
University of Rochester
University of Southern California
University of Southern Mississippi
University of Tennessee
University of Toronto
University of Vermont
University of Virginia
University of Washington
University of Wisconsin, Madison
Vanderbilt University
Virginia Tech
Washington University
Wayne State University
Williams College

Hospital/Medical School
AMC
Baylor College of Medicine
Beth Israel Deaconess Medical Center
Case Western Reserve University
Children's Hospital of The King's Daughters, Center for Pediatric Research
Clarian Health
Dana-Farber Cancer Institute
Duke University Medical Center
Emory University School of Medicine
Harvard Medical School
Hershey Medical Center
Hospital for Sick Children, Toronto
Institute of Human Virology, University of Maryland
Johns Hopkins Hospital
Johns Hopkins School of Medicine
Louisiana State University
LSU Health Sciences Center
LSU Health Sciences Center, Neuroscience Center
Mallory Institute of Pathology
Massachusetts General Hospital
Medical College of Ohio
Medical College of Virginia
Medical College of Wisconsin
Medical University of South Carolina
Memorial University of Newfoundland/Health Sciences Ctre
Michigan State University
New York University Medical Center
Northwestern University
Ohio State University Medical Center
Penn State Hershey Medical Center
Rush Medical Center
S Illinois University School of Medicine
Saint Louis University
SUNY Upstate Medical University
Texas A&M University College of Veterinary Medicine
University of Alabama Medical School
University of Arkansas for Medical Sciences
University of California, Davis School of Medicine
University of California, Los Angeles, Pediatric Endocrinology
University of California, San Diego
University of California, San Diego Medical Center
University of Cincinnati
University of Colorado Health Sciences Center
University of Florida
University of Georgia College of Veterinary Medicine
University of Louisville School of Medicine
University of Massachusetts Medical School
University of Medicine & Dentistry, New Jersey, RW Johnson Medical School

University of Minnesota
University of Mississippi Medical Center
University of North Carolina, Chapel Hill
University of Pennsylvania
University of Pittsburgh
University of Pittsburgh Medical School
University of Pittsburgh School of Medicine
University of South Dakota School of Medicine
University of South Florida
University of South Florida College of Medicine
University of Southern California
University of Tennessee
University of Texas Health Sciences Center, Houston
University of Texas Health Sciences Center, San Antonio
University of Texas Medical Branch
University of Wisconsin
UT Southwestern Medical School
Vanderbilt University Medical Center
Wake Forest University School of Medicine
Weill Cornell Medical College

Biotechnology/Pharmaceutical Industry

Abbott Laboratories
Acambis, Incorporated
Advanced Bioscience Laboratories
Astrazeneca R&D, Boston
Aventis Pharmaceuticals
Beckman Coulter, Inc.
Berkeley HeartLab, Inc.
Bioqual, Inc.
Bolder Biotechnology
Calgene
Cambria Biosciences
Chiron Corporation
Clingenix Inc.
Colgate-Palmolive
Eli Lilly and Company
ENZO Life Sciences
Essential Therapeutics
FDAH, Inc.
Fibrogen, Inc.
Gene Check, Inc
GeneDx Inc.
Genetic Therapy Inc.
Genzyme Corporation
Genzyme Transgenics Corporation
GlaxoSmithKline
Heska Corporation
Hoffmann-LaRoche Inc.

Intervet, Inc.
ISTA Pharmaceuticals
Koronis Pharmaceuticals
Ligand Pharmaceuticals
Lynx Therapeutics Inc
Merck & Company, Rahway
Merck Research Labs, West Point
Millennium Pharmaceuticals
Monsanto, Davis
Monsanto, Chesterfield
NeoRx Corporation
Nestor Motria Associates
Neurocrine
Neurome, Inc.
Novozymes Biotech, Inc
Osiris Therapeutics
Protein Design Labs, Inc.
Pfizer Corp, Cambridge
Pfizer Global R&D, Groton
Pharmacia Corporation
Procter & Gamble
Sigma-Aldrich
Stratagene
Third Wave Technologies
Torrey Mesa Research Institute/Syngenta
Wyeth Ayerst Research
Wyeth Vaccines

Government Agency

AFIP
Brookhaven National Laboratory
Centers for Disease Control and Prevention, Anchorage
Centers for Disease Control and Prevention, Atlanta
Centers for Disease Control and Prevention/NIOSH
Federal Drug Administration
James A Haley VA Medical Center
National Cancer Institutes, Frederick
National Cancer Institutes, Rockville
National Center for Toxicology Research
National Institutes of Health
National Institutes of Health/NEI
National Institutes of Health/NIAID
National Institutes of Health/NIEHS
National Institutes of Health/NINDS
National Institutes of Health/NIOSH
National Research Council Canada, Plant Biotechnology Institute
USDA Forest Service
USDA/Center for Veterinary Biologics, Ames
USDA/University of Missouri

USDA-ARS ANRI
USDA-ARS HCRL
USDA-ARS, Beltsville
USDA-ARS, Mississippi State
USUHS
VA Medical Center, Memphis
Walter Reed Army Institute for Research

Private Research Foundation

BSCS
Burnham Institute
Cedars-Sinai Medical Center
Henry Ford Health System
Jackson Laboratories
John Wayne Cancer Institute
Lahey Clinic
Mayo Clinic, Jacksonville
Mayo Clinic, Rochester
Mayo Foundation
MD Anderson Cancer Center
MedStar Research Institute
Memorial Sloan-Kettering Cancer Center
Nat'l Jewish Medical & Resch Center
Oklahoma Medical Research Foundation
Roswell Park Cancer Institute
Scripps Research Institute
Southwest Foundation for Biomedical Research
St. Jude Children's Research Hospital

Other Industry

Charles River Laboratories
IDNA Systems, Inc.
Nestle Purina Pet Care

QUESTION 2.

Question:

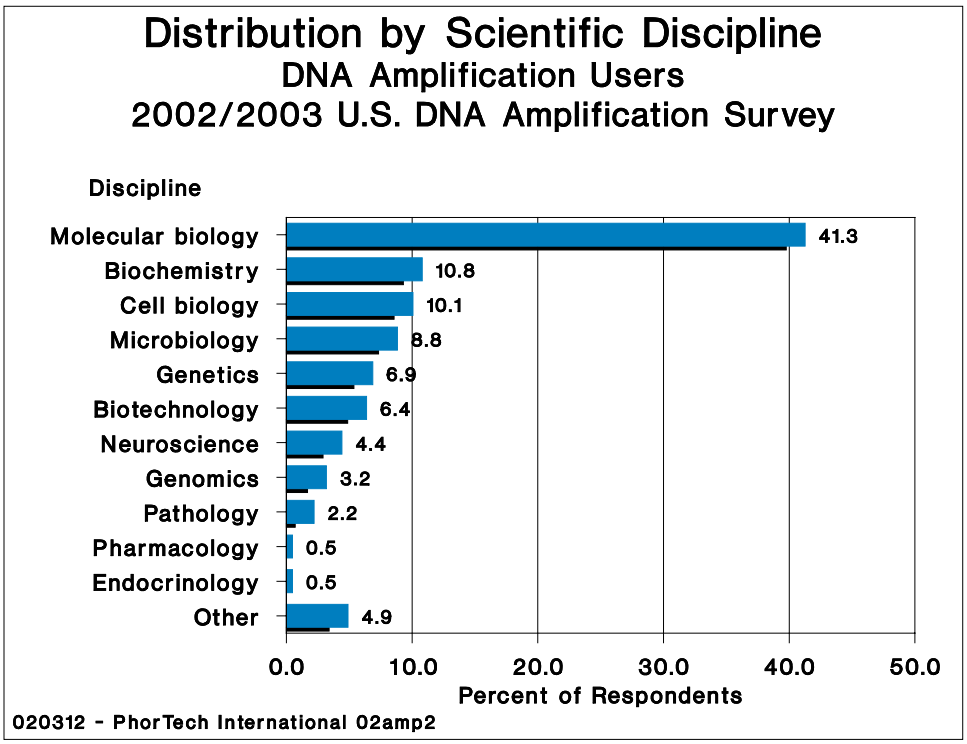
Please indicate below your primary scientific discipline.: *(Best single answer):* biochemistry, biotechnology, cell biology, endocrinology, genetics, genomics, microbiology, molecular biology, neuroscience, pharmacology, pathology or other?

Rationale:

The responses to this demographic screen will indicate the major disciplines of researchers performing DNA amplification. The choices reflect a balance between an exhaustive list of all possible life science categories and the most frequently-mentioned categories based upon previous work. Knowledge of the disciplines involved can give clients a good indication of the breadth of a particular technique.

Results:

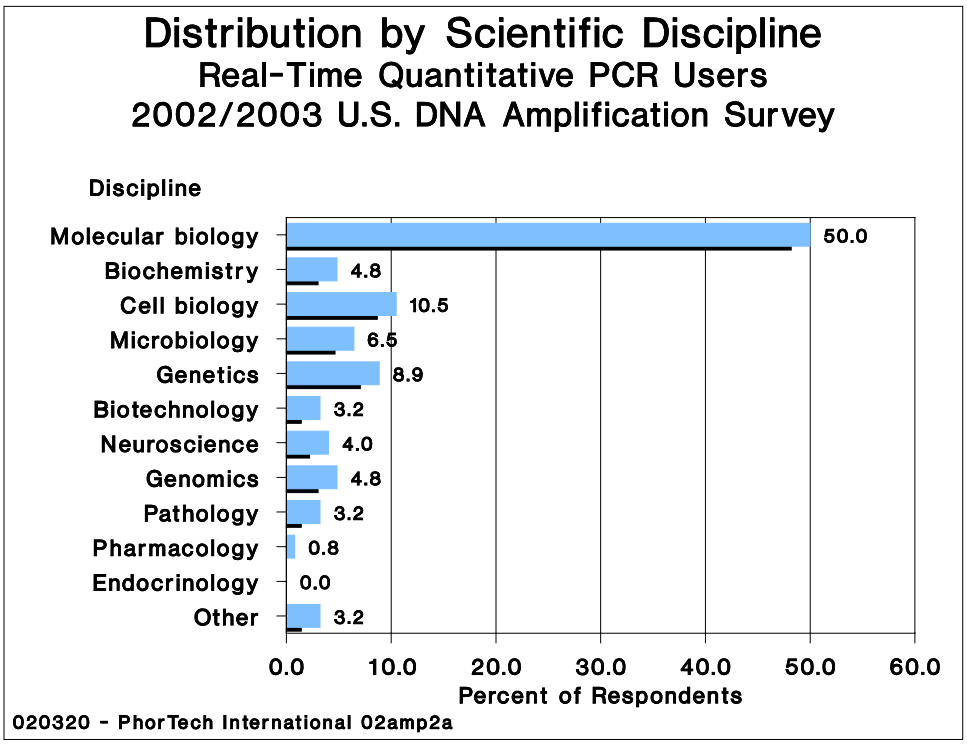
The following horizontal bar graph depicts the demographic profile of the 407 researchers currently using DNA amplification who answered this question.



Consistent with our previous studies in this area, the most common discipline is molecular biology. While this accounts for fully 40%,

dominating all other options, this is slightly lower than the near 55% share reported in our previous report on the U.S. DNA amplification market released in 1999.

Since, we have separated real-time quantitative PCR platforms for the first time, we also present the comparable distribution of the 124 researchers who perform this technique. The results are shown in the bar chart below.



Molecular biologist account for a slightly larger proportion of real time PCR users when compared with amplification users in general, and a slightly smaller proportion of scientists working primarily in biochemistry or biotechnology.

Analysis:

Molecular biology continues to be the primary discipline of researchers involved with DNA amplification. Each of the remaining 10 disciplines along with the 'other' category represents 10% or less for a combined total of 60% of respondents to this survey. This is very consistent with the results from our 1999 study in this area although we did note a doubling in the proportion of researchers involved with cell biology and genomics.

Researchers currently performing real time PCR are slightly more likely to be working in the area of molecular biology, and slightly less likely to be a biochemist. Amongst both DNA amplification users and real-time PCR

users, very few researchers indicate working in either pathology, pharmacology or endocrinology.

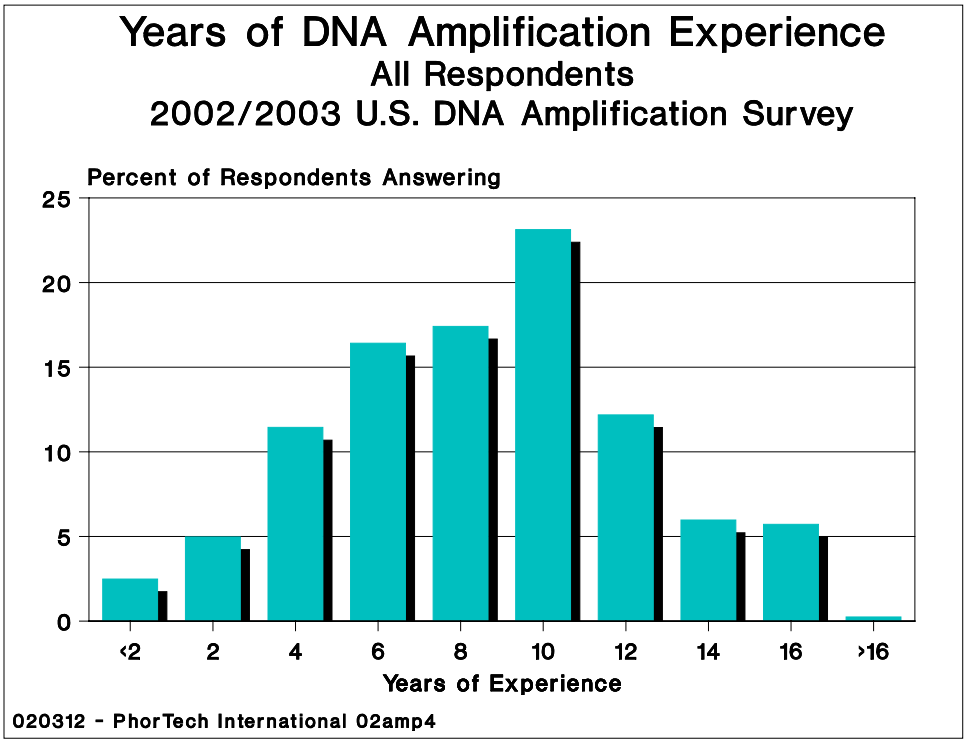
QUESTION 4.

Question:
How long *(in years)* have you been using DNA amplification?

Rationale:
This question allows us to determine respondents' level of experience with DNA amplification, as well as to investigate the expansion of this technique. Depending upon the results, we may be able to generate meaningful cross-tabulations for new versus highly experienced users.

Results:
The 402 respondents who answered this question report a wide variety of experience varying from zero to 20 years. Combined, these researchers represent a total of 3,263 years of experience. The 8.1 year average is nearly identical to the 8 year median and 10 year mode.

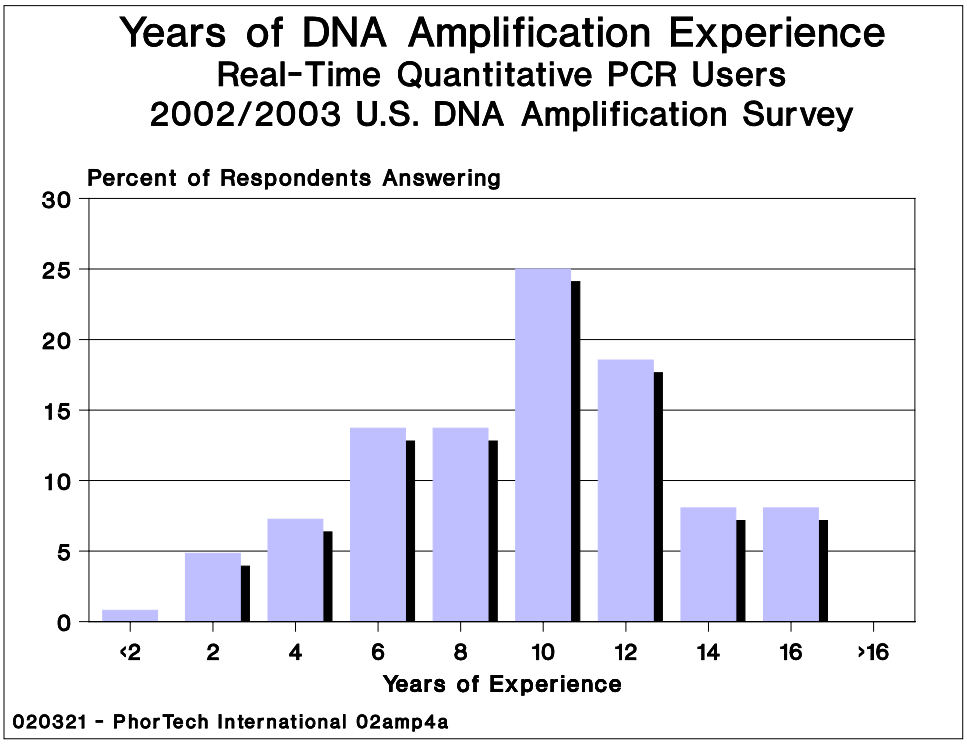
In the vertical bar chart below, we present the demographic profile for all respondents currently using DNA amplification, rounded up to the next year.



Only a small proportion, 7.5%, have performed DNA amplification for two years or less; by contrast, the majority, 57.0%, have between 5 and 10 years

of experience while 24.1% have been working in this area for more than 10 years.

As in the previous questions, we will also examine the responses for those 124 researchers who currently own or operate a platform for performing real time quantitative PCR. With a mean level of 9.0 years and a 10 year median and mode, these researchers appear to be slightly more experienced than DNA amplification users in general. The distribution of responses, depicted on the same scale as the previous graph and shown at the top of the next page, does appear to support this. In fact, fully one third, or 35.5% of real time PCR users report working with DNA amplification for more than 10 years, compared with 24.1% of all respondents.



Analysis:

Compared to the results from previous studies of this field, the 8.1 mean level of experience is very similar to the 7.8 year mean reported in our 1999 study, which was nearly double the 4.7 year mean found in 1995. This consistency reflects the maturity of this field. However, with the introduction of new applications, previously cycle sequencing, and currently, quantitative PCR and real-time PCR, this does not necessarily imply that the sales of thermal cyclers will decrease in the near future.